

regions, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, wherein said recombinant adenovirus genome additionally contains a transgene that replaces any one of said deletions.

N.E. 38. (twice amended) A replication-defective recombinant adenovirus, wherein the virus contains at least two lethal deletions, two lethal mutations, or one lethal deletion and one lethal mutation in the E1 and E4 early gene regions, wherein an essential region of the E4 early gene region is deleted or mutated, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, and wherein said recombinant adenovirus genome additionally contains a transgene that replaces any one of said deletions.

EX
FL 39. (thrice amended) A packaging cell line derived from a 293 cell that supports the growth of a replication defective recombinant adenovirus that carries at least two lethal deletions of adenovirus E1 and E4 early gene regions, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, comprising a cell line that supplies the function of the E1 early region and the E4 early region wherein nucleotide sequences encoding the E1 and E4 early regions are operably linked to an inducible promoter [and virus-associated RNA sequences].

NE 40. A DNA plasmid comprising an inducible promoter operably linked to nucleotide sequences encoding a cytotoxic gene product of an adenoviral E4 gene or E4 early gene region.

E2 41. (amended) The DNA plasmid of Claim 40 wherein said inducible promoter is [the] a promoter from [the] a cAMP response element binding protein regulated gene[s].

42. (amended) The DNA plasmid of Claim 41 wherein said inducible promoter is selected from [the] a gene encoding mammalian alpha inhibin.

43. (amended) The DNA plasmid of Claim 41 wherein said inducible promoter is selected from [the] a gene encoding mouse alpha inhibin.

44. (amended) The DNA plasmid of Claim [41] 40 wherein said inducible promoter is selected from [the] a gene encoding [the] a tetracycline responsive promoter.

45. The plasmid pIK6.1 MIP(2)-E4 designated ATCC #75879.

NE. 46. (twice amended) A recombinant adenoviral vector, wherein said vector comprises at least two lethal deletions, two lethal mutations or one lethal deletion or one lethal mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and additionally comprises a transgene that replaces any one of said deletions so that when rescued the resulting recombinant adenovirus

requires for replication complementation of genes of both the E1 and E4 adenoviral early regions.

7. E. 47. (twice amended) A recombinant adenoviral vector comprising at least two lethal deletions in the E1 and E4 early gene regions, and a transgene that replaces any one of said deletions so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

F² 48. (thrice amended) A packaging cell line derived from a 293-cell that supplies the function of the E4 early region wherein the nucleotide sequences encoding the E4 early region are operably linked to an inducible promoter and that supports the growth of a mutant adenovirus defective in replication, wherein said adenovirus comprises at least two lethal deletions, at least two lethal mutations, or at least one lethal mutation and one lethal deletion selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

49. (thrice amended) A packaging cell line derived from a 293 cell that supplies the function of the E4 early region wherein the nucleotide sequences encoding the E4 early region are operably linked to an inducible promoter and that supports the growth of a recombinant adenoviral vector comprising a transgene, wherein said vector comprises at least two lethal

F2
E2
deletions, two lethal mutations or one lethal deletion and one lethal mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

50. (thrice amended) A packaging cell line derived from a 293 cell that supplies the function of the E4 early region wherein the nucleotide sequences encoding the E4 early region are operably linked to an inducible promoter and that supports the growth of an adenoviral vector, wherein said vector comprises at least lethal two deletions selected from the group consisting of E1 and E4 early gene regions and a transgene that replaces any one of said deletions, so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

Claim 51 canceled.

nl.
52. The replication-defective recombinant adenovirus of Claim 38 in which the region of the E4 early gene region which is deleted or mutated is open reading frame 6.

Claim 53 canceled.